REMARKS/ARGUMENT

This response is submitted under 37 C.F.R. § 1.111 in reply to the Office Action of January 13, 2010.

Claims 2 through 5, 7 through 11, 14 through 17, and 20 through 23 are pending in the application. Claims 1, 6, 12, 13, 18, and 19 were previously canceled, and new claims 22 and 23 are added.

Claims 2 through 4, 14, and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Charles et al. (WO 00/46184).

Claims 5 through 11, 16, 17, 20, and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Charles et al. in view of Bennett (Goodman & Gillman, THE PHARMACEUTICAL BASIS OF THERAPEUTICS, 2001).

The Applicants incorporate WO 00/46184 by reference into the present specification. It is stated in paragraphs [0004] and [0005] of U.S. Publication No. 2006/0052459 (the published application of the present application):

> [0004] International application WO-00/46184 describes one or more N_2-phenylamidine derivatives. Such compounds are used in the agricultural field as antifungal agents.
>
> [0005] The applicant has demonstrated quite unexpectedly that N_2-phenylamidine derivatives also constituted antifungal compounds of choice, both in human being and in animal.

The Applicants, thus, do not deny that compositions disclosed in WO-00/46184 can be used in the practice of the present invention.

Charles et al. disclose that the compounds of their invention can be used to treat fungal infestations in domestic and farm animals.

Claim 16 is directed to a method for treating *Candida albicans* or *Aspergillus fumigatus* infections in *humans*. There is no disclosure or suggestion in Charles et al. that the compounds disclosed therein could be used for treating fungal infections in humans, nor is there any disclosure of the use of such compounds for treating *Candida albicans* or *Aspergillus fumigatus* infections in either humans or animals. Other than the single sentence referred to above, the Charles et al. disclosure is concerned only with the use of the compounds to combat fungi infestations in plants. Further, the only fungi specifically mentioned are *Phytophthora infestans, Plasmopara viticola, Erysiphe graminis*, *Leptosphaeria nodorum*, *Pyricularia oryzae, Pseudocercosporella herpotrichoides, Pellicularia sasakii, Botrytis cinerea, Rhizoctonia solani, Puccinia recondita, Venturia inaequalis*, and "other general pathogens of Deuteromycete, Ascomycete, Phycomycete and Basidomycete origin."

The Examiner has noted that "both *C. albicans* and *A. fumigatus* belong to the phylum Ascomycota, and are thus considered Ascomycetes." He is correct that both *C. albicans* and *A. fumigatus* belong to the phylum Ascomycota, but his attempt to use this fact as an argument for the obviousness of the present invention in view of Charles et al. is inapposite. *C. albicans* is a species of the subphylum Saccharomycotina, class Saccharomycetes, order Saccharomycetales, and family Saccharomycetaceae, whereas *A. fumigatus* is a species of the subphylum

Pezizomycotina, class Eurotiomycetes, order Eurotiales, and family Trichocomaceae.

Accordingly, they are quite different.

At the most, one might argue that it would be obvious to try using Charles et al.'s N^2-phenylamidine derivatives against members of the phylum Ascomycota, but it is well settled that "obvious to try" does not preclude patentability.

> An "obvious to try" rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success.

However,

> 'The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. . . . In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.'

MPEP 2145 X. B. (quoting *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988) (citations omitted). According to Microbeal Biorealm, an online microbiology resource,

> Ascomycota . . . is a recently discovered class. . . . This classification makes up more than75% of fungi. It is a very general category to describe a wide number of organisms, including yeasts. There are many famous and infamous organisms: *Saccharomyces cervisiae* (baker's yeast), *Penicillium chrysogenum* (penicillin), *Morchella esculentum* (morels), *Neurospora crassa* ("one-gene-one-enzyme" organism), *Aspergillus flavus* (aflatoxin), *Candida albicans* (which causes thrush, diaper rash, and vaginitis) and *Cryphonecrita parasitica* (a disease affecting chestnut trees) . . . .

http://microbewiki.kenyon.edu/index.php/Ascomycota (emphasis added).

Clearly the present case is a classic example of those for which "obvious to try" is not the standard under § 103, wherein "what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful."

It would require far more than undue experimentation for a person of ordinary skill in the art to determine that N^2-phenylamidine derivatives could be used in a method for treating *Candida albicans* or *Aspergillus fumigatus* infections in humans, based upon the teaching of Charles et al. that their compounds may be active against general pathogens of Deuteromycete, Ascomycete, Phycomycete and Basidomycete origin. It is respectfully submitted that it takes substantially more than that to render an invention anticipated or obvious. Seventy-five percent of all fungi is a lot of fungi.

All claims currently pending in the present application are dependent, either directly or indirectly, upon claim 16.

The Examiner has previously acknowledged that Charles et al. "do not teach a method combining compound I with another antifungal compound II, having a synergistic effect with a second compound, or further comprising a pharmaceutical excipient." It is thus understood to be the Examiner's position that Bennett supplements Charles et al. by showing that itraconazole and fluconazole are known compounds for the treatment of candidiasis and aspergillosis.

In paragraph [0114] of U.S. 2006/0052459, the Applicants stated:

> The objective of the trials is to test the efficacy of a compound of the arylamidine type, and two antifungal compounds of the family of azoles, fluconazole and itraconazole, already commercially available. These trials are aimed, in the first instance, at comparing the antifungal activity of the arylamidine type compound, taken alone, with that of azoles. Their aim is also to demonstrate the synergistic properties of the combinations of such compounds.

In other words, the arylamidine compounds that the Applicants are using are as good as, or better than, known compounds in the art.

This position is clearly demonstrated by the examples that follow, which are summarized in paragraphs [0137], [0138], [0143], and [0144]:

> [0137] The various results obtained and presented above demonstrate the efficacy of compound I.1, whether on minimal RPMI 1640 medium (MM) or on rich medium (RM), against Aspergillus fumigatus and Candida albicans with EC_{50} values between 0.1 and 0.5 μg/ml, and therefore having an activity equivalent to that of itraconazole (compound II.2) against Aspergillus fumigatus and an activity at least equivalent to that of fluconazole (compound II.1) against Candida albicans.
>
> [0138] As regards the interactions between compounds, the results obtained by the Wadley method show that the combination of compound I.1 and fluconazole (compound II.1) exhibits surprising synergistic effects both on Aspergillus fumigatus and on Candida albicans. The antifungal medicament according to the invention therefore constitutes real progress in terms of improvement of the antifungal activity compared with the references on the market.
>
> [0143] On Candida albicans, the EC_{50} of compound I.1 is 1.8 and 7.7 times higher than that of compounds II.1 and II.2, whereas compound I.2 shows better efficacy in vitro against Candida albicans than compounds I.1 and II.1.
>
> [0144] On Aspergillus fumigatus (IP 864.64), the EC_{50} of compound I.1 is about 700 times lower than that of compound II.1 and similar to that of compound II.2,

whereas compound I.2 shows efficacy in vitro on Aspergillus fumigatus twice higher than that of compounds I.1 and II.2.

Finally, on page 4 of the current Office Action, the Examiner acknowledged that, of the eight conditions disclosed in Table 6 of the specification, *three conditions demonstrate a synergistic effect.* It should be noted that new claims 22 and 23 are specifically directed to the combinations of Table 6 that produced the synergistic effect in the experimental work that was done.

Accordingly, it is requested that (1) rejection of claims 16, 5 through 11, and 17 through 21 under 35 U.S.C. § 103(a) as being unpatentable over Charles et al. in view of Bennett; and (2) rejection of claims 2 through 4, 14, and 15 under 35 U.S.C. § 103(a) as being unpatentable over Charles et al. be withdrawn.

In view of the foregoing, it is submitted that this application is now in condition. Favorable consideration is requested.

Respectfully submitted,

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Date

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